

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

CENTER FOR CANCER RESEARCH

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Dear Harold,

I received your recent letter and I report on our progress, or more realistically, the lack thereof. We have found the restriction enzyme business to be a bloody mess. It is apparent from all of our gel work that the proviral form I DNA is heterogeneous. With R_I we get some fragments but a fraction of the form I is R_I resistant! We have heard from Duesberg's lab that the fingerprint of our virus has a complexity of 9×10^6 ! As such, things do not appear to be as simple as we would have liked. We are presently recloning our stock with the hope of simplifying matters but I fear that Moloney leukemia may be an obligate heterozygote because of different defects in its different virion RNA subunits.

Although we didn't know the relative contributions of Guntaka etc. I feel badly about underplaying his role. We sent the paper off this week and I will attempt to change things at the proof stage if possible.

With regards to the non-circular forms, we realized that only a small portion of the material in the top band of EtBr gradient is really complete form II or III. We have an alkali gradient on which we will test both our ^{125}I and ^3H -cDNA probes. I think there must be quite a bit of single-stranded material there since we have found that a lot of the proviral DNA is hybridizable to ^{125}I in the absence of denaturation prior to the hybridization.

Concerning the genealogy of ideas, you might know that I worked for about 3 years on SV40, and still have a couple things going. We had and have been making SV40 DNA for a coupled transcription-translation project which we have here, and I have

been making 1.5 mg of SV40 form I at a time (compared with 0.01 µg of Moloney DNA)!! So I was running EtBr gradients until I was blue in the face. I had thus scheduled a series of characterizations of Moloney DNA, this being one of them. But in the end, talk is cheap, and what I had scheduled to do is irrelevant. What is relevant is the fact that you went ahead and did the experiment. There are always some people hanging around saying that they had thought of some experiments years before so-and-so went ahead and did it. I hope that I am not one of these a posteriori seers and if we appear as such in this manuscript, I will try to correct this in future work!

Best wishes,

A handwritten signature in dark ink, appearing to read "R. A. W.", with a stylized, cursive script.

RAW/mts

Robert A. Weinberg